L1 ANSWER 7 OF 10 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-172214 [16] WPIX
DOC. NO. CPI: C2000-053751 [16]
TITLE: New pyrimidinyl-substituted fused pyrazole derivatives,
used for treating cardiovascular disorders such as
hypertension, thromboembolic disease or ischemia
DERWENT CLASS: B02; B03
INVENTOR: ALONSO-ALIJA C; DEMBOWSKY K; FEURER A; HUETTER J; PERZBORN E; STAHL E; STASCH J; STRAUB A
PATENT ASSIGNEE: (FARB-C) BAYER AG; (FARB-C) BAYER HEALTHCARE AG
COUNTRY COUNT: 85

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| DE 19834047 | A1 | 20000203 | (200016)* | DE | 35[0] | |
| WO 2000006568 | A1 | 20000210 | (200016) | DE | | |
| AU 9952839 | A | 20000221 | (200029) | EN | | |
| EP 1102767 | A1 | 20010530 | (200131) | DE | | |
| JP 2002521482 | W | 20020716 | (200261) | JA | 116 | |
| US 6833364 | B1 | 20041221 | (200501) | EN | | |
| EP 1102767 | B1 | 20051102 | (200574) | DE | | |
| DE 59912742 | G | 20051208 | (200581) | DE | | |
| ES 2251213 | T3 | 20060416 | (200631) | ES | | |

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APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| DE 19834047 | A1 | ***DE 1998-19834047 | 19980729*** |
| AU 9952839 | A | AU 1999-52839 | 19990716 |
| DE 59912742 | G | DE 1999-512742 | 19990716 |
| EP 1102767 | A1 | EP 1999-938272 | 19990716 |
| EP 1102767 | B1 | EP 1999-938272 | 19990716 |
| DE 59912742 | G | EP 1999-938272 | 19990716 |
| WO 2000006568 | A1 | WO 1999-EP5073 | 19990716 |
| EP 1102767 | A1 | WO 1999-EP5073 | 19990716 |
| JP 2002521482 | W | WO 1999-EP5073 | 19990716 |
| US 6833364 | B1 | WO 1999-EP5073 | 19990716 |
| EP 1102767 | B1 | WO 1999-EP5073 | 19990716 |
| DE 59912742 | G | WO 1999-EP5073 | 19990716 |
| JP 2002521482 | W | JP 2000-562370 | 19990716 |
| US 6833364 | B1 | US 2001-744703 | 20010326 |
| ES 2251213 | T3 | EP 1999-938272 | 19990716 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO | |
|---|---|---|---|---|
| DE 59912742 | G | Based on | EP 1102767 | A |

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|---|---|---|---|---|
| AU 9952839 | A | Based on | WO 2000006568 | A |
| EP 1102767 | A1 | Based on | WO 2000006568 | A |
| JP 2002521482 | W | Based on | WO 2000006568 | A |
| US 6833364 | B1 | Based on | WO 2000006568 | A |
| EP 1102767 | B1 | Based on | WO 2000006568 | A |
| DE 59912742 | G | Based on | WO 2000006568 | A |
| ES 2251213 | T3 | Based on | EP 1102767 | A |

PRIORITY APPLN. INFO: DE 1998-19834047 19980729
AN 2000-172214 [16] WPIX
AB DE 19834047 A1 UPAB: 20060518
NOVELTY - 1-(Cyclic substituted methyl) 3-(cycloalkyl-substituted 2-pyrimidinyl) 4,5-fused pyrazole derivatives (I) are new.
DETAILED DESCRIPTION - Pyrazole derivatives of formula (I) and their isomers and salts are new.
At least one of R1, X, Y = saturated or partially unsaturated 3-8C cycloalkyl (optionally substituted (os) by one or more of NH2, N3, SH, COOH, OH, morpholino, piperidino, pyrrolidino, acyl, acylamino, alkoxy, alkylamino, up to 6C dialkylamino, alkylsulfonyl, alkylthio, up to 6C alkoxycarbonyl, NO2, CN, halo, Ph, or alkyl or cycloalkyl (optionally substituted by NH2, SH, COOH, morpholino, piperidino, pyrrolidino, acyl, acylamino, alkoxy, alkylamino, up to 6C dialkylamino, alkylsulfonyl, alkylthio, Ph, alkylsulfonylamino, up to 6C alkoxycarbonyl, NO2, CN or halo));
any other R1, X, Y = H or a very wide range of specific substituents;
R2 + R3 = group completing a phenyl ring or a 6-membered saturated or aromatic heterocycle (containing 1-3 of N, O and S), optionally substituted by a wide range of specific groups;
A = 5- or 6-membered saturated or aromatic heterocycle (containing 1-3 of N, O and S), optionally substituted by a wide range of specific groups;
unless specified otherwise alkyl, acyl and cycloalkyl moieties have up to 6C. Full definitions are given in the DEFINITIONS.
An INDEPENDENT CLAIM is included for the preparation of (I).
ACTIVITY - Cardiovascular; vascular relaxant; antithrombotic; hypotensive; coronary dilator; antiangina; antiarrhythmic; antiischemic; urogenital; neuroprotective; anxiolytic; antidepressant; analgesic.
3-(4-Amino-5-cyclopropylpyrimidin-2-yl)-1-(2-fluorobenzyl)-1H-pyrazolo

(3,4-b) pyridine (Ia) at 1 mg/kg p.o. gave a maximum blood pressure decrease of 23 mm Hg after 20 minutes in narcotized rats.

MECHANISM OF ACTION - Soluble guanyl cyclase stimulant; intracellular cyclic guanosine monophosphate (cGMP) level increasing agent. (I) also potentiates the activity of other agents which increase cGMP levels, e.g. endothelium derived relaxing factor (EDRF), nitrogen monoxide donors, protoporphyrin IX, arachidonic acid or phenylhydrazine derivatives.

USE - (I) cause vascular relaxation, inhibit thrombocyte aggregation, reduce blood pressure and increase coronary blood flow. They are used for treating cardiovascular disorders (claimed), e.g. hypertension, cardiac insufficiency, angina pectoris, peripheral or cardiac vascular disease, arrhythmia, thromboembolic disease or ischemia (claimed) (e.g. myocardial infarction, cerebral stroke, transitory ischemic attacks, peripheral blood flow disorders or restenosis), arteriosclerosis or diseases of the urogenital system (e.g. prostate hypertrophy, erectile dysfunction, female sexual dysfunction or incontinence). (I) are also useful for treating central nervous system disorders, especially for alleviating cognitive deficiency, improving learning and memory performance or treating Alzheimer's disease but also for treating anxiety, stress, depression, CNS-related sexual dysfunction, sleep disorders or food, condiment and sweetener uptake disorders. (I) are further useful for regulating cerebral blood flow, treating migraine or pain and treating or preventing the sequelae of cerebral infarction (e.g. stroke), cerebral ischemia or cranial-cerebral trauma.

Member(0002)

ABEQ WO 2000006568 A1 UPAB 20060518

NOVELTY - 1-(Cyclic substituted methyl) 3-(cycloalkyl-substituted 2-pyrimidinyl) 4,5-fused pyrazole derivatives (I) are new.

DETAILED DESCRIPTION - Pyrazole derivatives of formula (I) and their isomers and salts are new.

At least one of R1, X, Y = saturated or partially unsaturated 3-8C cycloalkyl (optionally substituted (os) by one or more of NH2, N3, SH, COOH, OH, morpholino, piperidino, pyrrolidino, acyl, acylamino, alkoxy, alkylamino, up to 6C dialkylamino, alkylsulfonyl, alkylthio, up to 6C

alkoxycarbonyl, NO2, CN, halo, Ph, or alkyl or cycloalkyl (optionally substituted by NH2, SH, COOH, morpholino, piperidino, pyrrolidino, acyl, acylamino, alkoxy, alkylamino, up to 6C dialkylamino, alkylsulfonyl, alkylthio, Ph, alkylsulfonylamino, up to 6C alkoxycarbonyl, NO2, CN or halo));

any other R1, X, Y = H or a very wide range of specific substituents;

R2 + R3 = group completing a phenyl ring or a 6-membered saturated or aromatic heterocycle (containing 1-3 of N, O and S), optionally substituted by a wide range of specific groups;

A = 5- or 6-membered saturated or aromatic heterocycle (containing 1-3 of N, O and S), optionally substituted by a wide range of specific groups;

unless specified otherwise alkyl, acyl and cycloalkyl moieties have up to 6C. Full definitions are given in the DEFINITIONS.

An INDEPENDENT CLAIM is included for the preparation of (I).

ACTIVITY - Cardiovascular; vascular relaxant; antithrombotic; hypotensive; coronary dilator; antiangina; antiarrhythmic; antiischemic; urogenital; neuroprotective; anxiolytic; antidepressant; analgesic.

3-(4-Amino-5-cyclopropylpyrimidin-2-yl)-1-(2-fluorobenzyl)-1H-pyrazolo (3,4-b) pyridine (Ia) at 1 mg/kg p.o. gave a maximum blood pressure decrease of 23 mm Hg after 20 minutes in narcotized rats.

MECHANISM OF ACTION - Soluble guanyl cyclase stimulant; intracellular cyclic guanosine monophosphate (cGMP) level increasing agent. (I) also potentiates the activity of other agents which increase cGMP levels, e.g. endothelium derived relaxing factor (EDRF), nitrogen monoxide donors, protoporphyrin IX, arachidonic acid or phenylhydrazine derivatives.

USE - (I) cause vascular relaxation, inhibit thrombocyte aggregation, reduce blood pressure and increase coronary blood flow. They are used for treating cardiovascular disorders (claimed), e.g. hypertension, cardiac insufficiency, angina pectoris, peripheral or cardiac vascular disease, arrhythmia, thromboembolic disease or ischemia (claimed) (e.g. myocardial infarction, cerebral stroke, transitory ischemic attacks, peripheral blood flow disorders or restenosis),

arteriosclerosis or diseases of the urogenital system (e.g. prostate hypertrophy, erectile dysfunction, female sexual dysfunction or incontinence). (I) are also useful for treating central nervous system disorders, especially for alleviating cognitive deficiency, improving learning and memory performance or treating Alzheimer's disease but also for treating anxiety, stress, depression, CNS-related sexual dysfunction, sleep disorders or food, condiment and sweetener uptake disorders. (I) are further useful for regulating cerebral blood flow, treating migraine or pain and treating or preventing the sequelae of cerebral infarction (e.g. stroke), cerebral ischemia or cranial-cerebral trauma.

Member(0004)
ABEQ EP 1102767 A1 UPAB 20060518
NOVELTY - 1-(Cyclic substituted methyl) 3-(cycloalkyl-substituted 2-pyrimidinyl) 4,5-fused pyrazole derivatives (I) are new.
DETAILED DESCRIPTION - Pyrazole derivatives of formula (I) and their isomers and salts are new.
At least one of R1, X, Y = saturated or partially unsaturated 3-8C cycloalkyl (optionally substituted (os) by one or more of NH2, N3, SH, COOH, OH, morpholino, piperidino, pyrrolidino, acyl, acylamino, alkoxy, alkylamino, up to 6C dialkylamino, alkylsulfonyl, alkylthio, up to 6C alkoxycarbonyl, NO2, CN, halo, Ph, or alkyl or cycloalkyl (optionally substituted by NH2, SH, COOH, morpholino, piperidino, pyrrolidino, acyl, acylamino, alkoxy, alkylamino, up to 6C dialkylamino, alkylsulfonyl, alkylthio, Ph, alkylsulfonylamino, up to 6C alkoxycarbonyl, NO2, CN or halo));
any other R1, X, Y = H or a very wide range of specific substituents;
R2 + R3 = group completing a phenyl ring or a 6-membered saturated or aromatic heterocycle (containing 1-3 of N, O and S), optionally substituted by a wide range of specific groups;
A = 5- or 6-membered saturated or aromatic heterocycle (containing 1-3 of N, O and S), optionally substituted by a wide range of specific groups;
unless specified otherwise alkyl, acyl and cycloalkyl moieties have up to 6C. Full definitions are given in the DEFINITIONS.

An INDEPENDENT CLAIM is included for the preparation of (I).

ACTIVITY - Cardiovascular; vascular relaxant; antithrombotic; hypotensive; coronary dilator; antiangina; antiarrhythmic; antiischemic; urogenital; neuroprotective; anxiolytic; antidepressant; analgesic. 3-(4-Amino-5-cyclopropylpyrimidin-2-yl)-1-(2-fluorobenzyl)-1H-pyrazolo (3,4-b) pyridine (Ia) at 1 mg/kg p.o. gave a maximum blood pressure decrease of 23 mm Hg after 20 minutes in narcotized rats.

MECHANISM OF ACTION - Soluble guanyl cyclase stimulant; intracellular cyclic guanosine monophosphate (cGMP) level increasing agent. (I) also potentiates the activity of other agents which increase cGMP levels, e.g. endothelium derived relaxing factor (EDRF), nitrogen monoxide donors, protoporphyrin IX, arachidonic acid or phenylhydrazine derivatives.

USE - (I) cause vascular relaxation, inhibit thrombocyte aggregation, reduce blood pressure and increase coronary blood flow. They are used for treating cardiovascular disorders (claimed), e.g. hypertension, cardiac insufficiency, angina pectoris, peripheral or cardiac vascular disease, arrhythmia, thromboembolic disease or ischemia (claimed) (e.g. myocardial infarction, cerebral stroke, transitory ischemic attacks, peripheral blood flow disorders or restenosis), arteriosclerosis or diseases of the urogenital system (e.g. prostate hypertrophy, erectile dysfunction, female sexual dysfunction or incontinence). (I) are also useful for treating central nervous system disorders, especially for alleviating cognitive deficiency, improving learning and memory performance or treating Alzheimer's disease but also for treating anxiety, stress, depression, CNS-related sexual dysfunction, sleep disorders or food, condiment and sweetener uptake disorders. (I) are further useful for regulating cerebral blood flow, treating migraine or pain and treating or preventing the sequelae of cerebral infarction (e.g. stroke), cerebral ischemia or cranial-cerebral trauma.